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MARSH, FISCHMANN & BREYFOGLE LLP
8055 East Tufts Avenue
Suite 450
Denver, CO 80237

EXAMINER	
LI, BAO Q	

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOAN P. BLONDER, CLAIRE M. COESHOTT, TIMOTHY C. RODELL, WREN H. SCHAUER, and GARY J. ROSENTHAL

Appeal 2009-013898
Application 09/888,235
Technology Center 1600

Decided: December 11, 2009

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and STEPHEN WALSH, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 1, 4-7, 9-31, 33-37, 39-44, 148, and 149, the only claims pending in this application (Reply Br. 2). We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

The claims are directed to a composition (claims 1, 4-7, 9-31, 33-37, 39-43, 148, and 149) and a method of packaging and storing the composition of claim 5 (claim 44). Claim 1 is illustrative[1]:

1. A composition for delivery of an antigen for stimulation of an immune response when administered to a host, the composition comprising:

an antigen, a polyoxyalkylene block copolymer and an aqueous liquid;

the polyoxyalkylene block copolymer being biocompatible, not having toxic or injurious effects on biological function in the host when the composition is administered;

wherein, the composition is formulated with relative proportions of the liquid and the copolymer so that the copolymer interacts with the liquid to impart reverse thermal viscosity behavior to the composition, so that the viscosity of the composition increases when the temperature of the composition increases over some temperature range within 1°C to 37°C; and

wherein, the composition further comprises an additive enhancing the immune response when the composition is administered to the host, the additive being an adjuvant other than alum;
and;

wherein, the liquid comprises from 60 weight percent to 85 weight percent of the composition, the antigen comprises from 0.0001 weight percent to 5 weight percent of the composition, the copolymer comprises from 5 weight percent to 33 weight percent of the composition and the additive comprises from 0.01 weight percent to 10.0 weight percent of the composition.

The Examiner relies on the following evidence:

Viegas	US 5,300,295	Apr. 5, 1994
Hale	US 5,607,691	Mar. 4, 1997
Alonso	EP 0 860 166 A1	Aug. 26, 1998

[1] A correct version of the claims appears in the appendix of Appellants' Reply Brief.

Appellants rely on the following evidence:

Coeshott Declaration, executed April 22, 2003.

Cha	US 5,702,717	Dec. 30, 1997
Stratton	US 5,861,174	Jan. 19, 1999

Newman, *Development of adjuvant-active nonionic block copolymers*, 32 Adv. Drug Delivery Rev. 199-223 (1998).

The rejection presented by the Examiner follows:

Claims 1, 4-7, 9-31, 33-37, 39-44, 148, and 149 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Alonso, Hale, and Viegas.

We reverse.

ISSUE

Have Appellants established error in the Examiner's prima facie case of obviousness?

FINDINGS OF FACT

FF 1. Alonso teaches "nanoparticles based on hydrophilic polymers as pharmaceutical forms for the administration of bioactive molecules" (Alonso 2: 3-4).

FF 2. The Examiner finds that Alonso teaches an immunogenic composition comprising an antigen (diphtheria toxoid), an adjuvant additive (chitosan), a polyoxyalkylene block copolymer (PEO or PEO-PPO) and water (Ans. 4).

FF 3. Alonso teaches that "[t]he size of the nanoparticles is mainly dependent on the chitosan concentration in the nanoparticles formation medium. Thus, for a very low chitosan aqueous concentration (lower than 0.01%) or a very high chitosan aqueous concentration (higher than 0.5%), an aqueous gel solution or a suspension of microparticles (larger than 1 μm)_is formed respectively" (Alonso 3: 37-40). Alonso provides examples of nanoparticles prepared by a formulation having a 0.14% chitosan content (*Id.* at 4-5).

FF 4. Alonso teaches that:

> The formation of the nanoparticles occurs spontaneously due to the simultaneous precipitation of chitosan and the bioactive macromolecule caused by the incorporation of a molecule with a basic character, i.e. sodium tripolyphosphate (counter anion). This process can be also considered as a process of ionic gelation or ionic croslinking [sic] of chitosan with the counter anion.

(Alonso 2: 23-26.)

FF 5. Alonso teaches that "the size of the particles can be also modulated by incorporating PEO or PEO-PPO in the nanoparticles formation medium" (Alonso 3: 40-41).

FF 6. Alonso teaches "augmentation in the nanoparticle size (from 275 nm to 685 nm) caused by the incorporation of increasing amounts of PEO-PPE in the medium (the chitosan/PEO-PPO ratio varied from 1/0 up to 1/50)" (Alonso 3: 42-44).

FF 7. Using a chitosan/PEO-PPE ratio of 1/50, the Examiner finds that Alonso teaches a composition comprising approximately 93% (w/w) water, about 0.014% (w/w) antigen, 7% (w/w) polyoxyalkylene block copolymer, and about 0.14% (w/w) of adjuvant (chitosan) (Ans. 4).

FF 8. The Examiner finds that Alonso does "not explicitly teach the general structure and reverse thermal sensitivity of said PEO-PPO block copolymer" (Ans. 6).

FF 9. Viegas teaches "[a]queous gel drug delivery compositions" (Viegas, Abstract).

FF 10. The Examiner finds that Viegas teaches "a therapeutic composition comprising a reverse thermal sensitive block copolymer, wherein said block copolymer is selected from [a] wide variety of polyoxyalkelene [sic] copolymers (PEO-PPO) that exhibit . . . reverse thermal viscosity characteristics, i.e., being a low viscosity at ambient temperature . . . but forms a semisolid gel at mammalian body temperatures" (Ans. 6).

FF 11. The Examiner finds that Viegas teaches that Pluronic® F127, is a polyoxalkylen[e] copolymer that "is suitable for preparing a pharmaceutical composition that exhibits the reverse thermal viscosity property, wherein the concentration of said polyoxalkylen[e] block copolymer var[ies] greatly from 2% to 50% or even higher" (Ans. 7).

FF 12. Based on the teachings of Viegas, the Examiner finds that prior to Appellants' filing date, the art recognized that PEO-PPO block copolymer exhibited reverse thermal viscosity properties (Ans. 7).

FF 13. Therefore, the Examiner finds that "[t]he only . . . difference between the claims and the composition disclosed by Alonso et al. is the 7~8% more water [i.e., liquid] than" is required by Appellants' claimed invention (Ans. 7).

FF 14. The Examiner relies on Hale to teach the delivery of a pharmaceutical composition comprising a biological protein or peptide molecule via an aerosol spray (Ans. 8).

PRINCIPLES OF LAW

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992). On appeal to this Board, Appellants must show that the Examiner has not sustained the required burden. *See Ex parte Yamaguchi*, 88 USPQ2d 1606, 1608 and 1614 (BPAI 2008) (precedential); *Ex parte Fu*, 89 USPQ2d 1115, 1118 and 1123 (BPAI 2008) (precedential).

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). It is proper to "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418. *See also id.* at 421 ("A person of ordinary skill is also a person of ordinary creativity, not an automaton."). In sum, the "suggestion test is in actuality quite flexible and not only permits, but *requires*, consideration of common knowledge and common sense." *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006).

Nevertheless, an invention "composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. . . . [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, 550 U.S. at 418.

ANALYSIS

Appellants' claimed invention is drawn to a composition comprising, *inter alia*, an additive being an adjuvant additive (e.g., chitosan) and a polyoxyalkylene block copolymer (Claim 1). Appellants' claim 1 requires the composition to be formulated with relative proportions of liquid and copolymer so that the copolymer interacts with the liquid to impart reverse thermal viscosity behavior to the composition. As a result claim 1 requires the viscosity of the composition to increase when the temperature of the composition increases over some temperature range within 1°C to 37°C (*id.*).

The Examiner relies on Alonso to teach an immunogenic composition comprising an antigen (diphtheria toxoid), an adjuvant additive (chitosan), a polyoxyalkylene block copolymer (PEO or PEO-PPO) and water (FF 2). The Examiner relies on Viegas to establish that PEO-PPO block copolymers that exhibit reverse thermal viscosity properties were known in the art at the time of Appellants' invention (FF 9-12). Therefore, the Examiner concludes that "in order to make an immunogenic composition with more biocompatibilities, it would have been obvious for a person of ordinary skill in the art to make an immunogenic composition taught by Alonso et al. with a reverse thermal viscosity property by using the PEO-PPO copolymer taught by Viegas et al." (Ans. 8). We are not persuaded.

Alonso's composition is formulated to spontaneously form nanoparticles (FF 1 and 4 ("[t]he formation of the nanoparticles occurs spontaneously due to the simultaneous precipitation of chitosan and the bioactive macromolecule caused by the incorporation of a molecule with a basic character, i.e. sodium tripolyphosphate (counter anion)"). Viegas teaches "[a]queous gel drug delivery compositions" (FF 9).

Appellants contend that "[t]he nanoparticles of *Alonso et al.* and the temperature-sensitive gelling compositions of *Viegas et al.* are structurally very different types of drug delivery approaches, so different that they would not logically be considered as susceptible to combination by those of ordinary skill in the art" (App. Br. 38). We agree.

While Alonso teaches that an aqueous gel solution can be obtained with "a very low chitosan aqueous concentration (lower than 0.01%)" (FF 3), this concentration is below: (a) the concentration required by Appellants' claimed invention (*see* Appellants' claim 1 (wherein the additive (e.g., chitosan concentration) is from 0.01 weight percent to 10.0 weight percent)) and (b) the chitosan concentration of "about 0.14% (w/w)" relied upon by the Examiner (FF 7). In addition, the Examiner provides no evidence to support a conclusion that Viegas' PEO-PPO block copolymers will continue to exhibit their reverse thermal viscosity property in the context of a nanoparticle composition formulated by Alonso.

The obviousness analysis does not end with a finding that Alonso's composition includes some of the same ingredients, in the same concentration, as required by Appellants' claimed invention. To the contrary, the analysis must go further to determine whether the formulation of Alonso's composition, modified as proposed by the Examiner, would have been expected to result in a composition that exhibits the properties required by Appellants' claims. *See, e.g.*, Appellants' claim 1, which requires the composition to be "formulated with relative proportions of the liquid and the copolymer so that the copolymer interacts with the liquid to impart reverse thermal viscosity behavior to the composition, so that the

viscosity of the composition increases when the temperature of the composition increases over some temperature range within 1°C to 37°C."

At best, the Examiner asserts that "regardless whether the chitosan with copolymer forms a nanoparticle or not, the composition, especially the nanoparticle having a size at 685±27 nm comprises the same active ingredients and at least the major immunological and pharmaceutical active components are in the same ranges as" set forth in Appellants' claims (Ans. 11). The Examiner does not, however, provide an evidentiary basis to support a conclusion that a person of ordinary skill in the art would have expected such a formulation to exhibit the properties required by Appellants' claimed invention. The Examiner also relied on ordinary optimization to arrive at the claimed formulation, but we are not persuaded and we agree with Appellants' analysis. *See* Reply Br. at 8.

Demonstrating that each of the elements of Appellants' claimed invention was, independently, known in the prior art is not sufficient. Instead, an important aspect of an obvious determination is the identification of a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *KSR*, 550 U.S. at 418. For the reasons set forth above, the Examiner failed to provide a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does (*See e.g.,* Reply Br. 8-9).

Hale fails to make up for the deficiencies in the combination of Alonso and Viegas.

CONCLUSION OF LAW

Appellants established error in the Examiner's prima facie case of obviousness. The rejection of claims 1, 4-7, 9-31, 33-37, 39-44, 148, and 149 under 35 U.S.C § 103(a) as unpatentable over the combination of Alonso, Hale, and Viegas is reversed.

REVERSED

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MARSH, FISCHMANN & BREYFOGLE LLP
8055 EAST TUFTS AVENUE
SUITE 450
DENVER, CO 80237